

CLAIMS

1. A pharmaceutical composition of small-sized, unilamellar liposomes, for parenteral administration of an active compound, comprising: liposomes with an average diameter from about 75 nm to about 300 nm, wherein the unilamellar membrane contains a mixture of saturated lipids, said unilamellar membrane containing at least one lysophospholipid in an amount of about 0,5 mol% to 6.0 mol% regarding the total lipid content, and a therapeutic encapsulated compound included inside said liposomes.
2. A composition according to claim 1, wherein the lysophospholipid is selected from lysophosphatidylcholine, lysophosphatidylinositol, lysophosphatidylserine and lysophosphatidic acid or combinations thereof.
3. A composition according to claim 1, wherein the saturated lipids are selected from phosphatidylcholine, cholesterol, phosphatidylethanolamine, phosphatidylinositol, phosphatidylglycerol, natural phosphatidylcholine (soy and/or egg), distearoyl phosphatidylethanolamine derivatized with O - methylated polyethyleneglycol 750-5000, dipalmitoyl phosphatidylethanolamine derivatized with O-methylated polyethyleneglycol 750-5000 or combinations thereof.
4. A composition according to claim 3, wherein distearoyl phosphatidylethanolamine is derivatized with O-Methyl-polyethylene-glycol 2000
5. A composition according to claim 3, wherein dipalmitoyl phosphatidyl ethanolamine is derivatized with O-methyl-polyethylene-glycol 2000
6. A composition according to claim 1, wherein the active principle is a cytotoxic agent.
7. A composition according to claim 6, wherein the

cytotoxic agent is selected from anthracyclenic antibiotics, taxanes and platinum salts.

8. A composition according to claim 7, wherein the anthracyclenic antibiotic is selected from the group
5 consisting in doxorubicin, epirubicin and daunorubicin and pharmaceutically acceptable salts thereof.

9. A pharmaceutical composition of unilamellar, small sized liposomes for parenteral administration of an active compound, according to claim 1, comprising:
10 liposomes with an average diameter from about 75 nm to about 300 nm, wherein said unilamellar membrane contains a mixture of saturated lipids, comprising at least one lysophospholipid in an amount of about 0,5 mol% to about 6,0 mol% related to the total lipid
15 content, and encapsulated doxorubicin inside said liposomes in a ratio of about 8,5% by weight to about 11,5% by weight related to the total weight of lipids in the liposomes.

10. A method of preparing a composition according to
20 claim 1, comprising the steps of: forming liposomes from a solution containing saturated lipids and at least a lysophospholipid in an amount of about 0,5 mol% and 6,0 mol% regarding the total lipid content, and evaporation to dryness; taking the film up in
25 aqueous solution; submitting the foregoing solution to freezing and thawing cycles extruding through membranes of decreasing pore up to a membrane of 50 nm pore, obtaining liposomes with an average diameter of about 75 nm to about 300 nm, dialyzing the liposome
30 suspension, and mixing the dialyzed liposome suspension with a solution of the active compound.

11. A method according to claim 10, wherein the lysophospholipid is selected among
lysophosphatidylcholine, lysophosphatidylinositol,
35 lysophosphatidylserine and lysophosphatidic acid.

12. A method of preparing a composition of claim 9, comprising the steps of: forming liposomes from a solution containing saturated lipids and at least a lysophospholipid in an amount of about 0,5 mol% to 6,0 mol% regarding the total lipid content, and evaporating to dryness; taking the film up in a solution of an ammonium salt; submitting the foregoing solution to freezing and thawing cycles extruding through membranes of decreasing pore up to a membrane of 50 nm pore, obtaining liposomes with an average diameter of about 75 nm to about 300 nm; dialyzing the liposome suspension against an aqueous solution without ammonium ions; mixing the dialyzed liposome suspension with a solution of about 50 mM to about 200 mM of a soluble calcium salt and a solution of doxorubicin at a concentration of about 2 to about 30 mg/ml, obtaining a percentage of more than 80% of encapsulation of doxorubicin.

13. A method according to claim 12, wherein the calcium salt is calcium chloride.

14. A method according to claim 12 or 13, wherein the volume ratio of calcium chloride solution to doxorubicin solution is of 1:10 (v:v).

15. A method according to claim 12, wherein the percentage of encapsulated doxorubicin increases between 20 to 70% in the presence of calcium chloride, compared to a method which does not use calcium chloride.